New claims 22-34 are added.

New claims 22 and 23 are dependent upon claim 13. New claim 22 is identical to original claim 15 in USSN 08/459,654 (which had been canceled in the prior application). New claim 23 includes a limitation which further limits the value of m in the claim 13 structure.

New claim 24 is directed to a "substantially pure preparation of an inhibitor of DP-IV" which has the structure of amended claim 13. Support for this new claim is found at least on page 21 (line 12) which describes the purification procedure that was used to obtain "an isomeric purity of about 99-6% for each isomer".

New claim 25 is directed to the preparation of claim 24 with the further limitation that the inhibitor is present at 99% purity. Support for this new claim also is found on page 21.

New claims 25-30 parallel original claims 14-18 and new claim 23 which further specify limitations of the DP-IV inhibitor. Accordingly, support for these claims is found at least in original claims 14-18 as filed.

Claim 31 is directed to the structure of claim 13 which has been modified to include a carboxyl terminal functional group which is selected from the groups consisting of the boronates (the subject matter of claim 13), the phosphonates (the subject matter of new claim 32), and the trifluoroalkyl ketones (the subject matter of new claim 33). Support for new claims 31, 32, and 33 is found at least beginning on page 5 of the specification which describes the different types of T groups that can be present at the C terminal end of the molecule.

Claim 34 is directed to a method for inhibiting DP-IV which involves contacting DP-IV with the inhibitor of claim 31 under conditions to permit binding of the inhibitor to the DP-IV. Support for this new claim is found at least in original claim 11 as filed.

Remarks Concerning the Outstanding Rejections in the Parent Case, USSN 08/459,654

The following information is provided to expedite the prosecution of this file wrapper continuation of USSN 08/459,654:

Applicants are in the process of compiling a complete list of references which may be relevant to the subject matter that is claimed in this pending application. These references were identified in related patent applications or were identified in general searches of the literature and patent databases. Applicants shall make this information of record within three months of filing this file-wrapper-continuation. Not all of the references cited may be prior art with respect to the claimed invention, i.e., certain references may have been published after the earliest effective filing date of this pending file-wrapper-continuation application. In addition, certain of the references may have been filed within one year of the filing of the earliest effective application to which priority is claimed and, therefore it is possible that a declaration under 37 C.F.R. §1.131 could remove certain references as prior art. For example, Applicants have evidence available to submit in the form of a section 1.131 Declaration for the purpose of removing as prior art, the reference by W. Bachovchin, et al., in J. Biol. Chem. 265(7):3738 (1990), which describes certain DP-IV isomers. This information will be provided upon request by the Examiner.

Applicants have added new claims to inhibitors of DP-IV and methods of using said inhibitors. Certain of the new claims define the purity of the originally claimed DP-IV inhibitor (claim 13); other claims define DP-IV inhibitors in which the carboxyl terminal group contains a functional group which is a boronate groups (as in original claim 13), a phosphonate group or a trifluoroalkyl ketones. Applicants respectfully request that the Examiner consider the patentability of these new claims. Support for the new claims is provided in the specification on the pages identified above.

The undersigned attorney has noted the objection to the Abstract's length and

claims.

The following comments are specifically directed to the outstanding claim rejections in the parent application.

A rejection of claims under 35 U.S.C. §112(1) in USSN 08/459,654 appears to be based on "scientific reasoning", namely, that a non-conservative amino acid substitution at positions A or A' in the formula of claim 13 would result in a "loss of activity" . Applicants note that the pending claims do not specify a particular *level* of activity, merely a composition which is in a particular isomeric form. That compounds which fall within the claim may have different *levels* of activity is not a sufficient basis to reject the claim for a lack of enablement. Moreover, Applicants have in their possession experimental or other evidence to support their position that DP-IV inhibitors will tolerate a broad spectrum of substitutions for amino acids in positions A and A′ of claim 13. Upon request by the Examiner, Applicants will provide this information in the form of a declaration under 35 U.S.C. §1.132 to expedite the prosecution of this continuation.

With respect to the rejection of claims under 35 U.S.C. §112(2) in USSN 08/459,654, it is believed that this rejection is obviated by the amendments submitted herewith.

The pending claims of USSN 08/459,654 also were rejected under 35 U.S.C. §102(e) as anticipated by Bachovchin (US Patent No. 4,935,493). This rejection is based upon an interpretation that the Bachovchin patent is "silent as to the stereochemical disposition of the α-carbon" and, accordingly, that Bachovchin shows the L-isomer. Respectfully, Bachovchin is *not* silent as to the stereochemical disposition of this carbon atom. Rather, Bachovchin clearly states (column 7, lines 67-68): "all natural amino acids are in the L-configuration. H-boroProline is in the D, L-configuration". Accordingly, Bachovchin does not teach a substantially pure

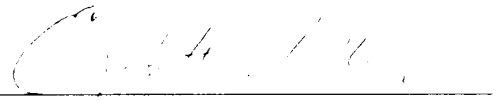
Respectfully , one would expect that a mixture which contains 100% of an active compound would be approximately twice as active as a mixture which contains only 50% of the active compound (a racemic mixture). In contrast to such expectations, the specification (page 21, line 29) discloses that the inhibition constant for the L-isomer of proBoroPro was approximately *three orders of magnitude* better than the D-isomer for this same dipeptide. This difference was pointed out in the Amendment filed on February 26, 1997 by Applicants' former representative. Compounds which have such unexpected properties are, by their nature, inherently nonobvious. For this additional reason, it is believed that the Bachovchin patent does not teach, suggest, or render obvious the invention as now claimed.

## SUMMARY

Applicants which to expedite the prosecution of this application. Accordingly, if the Examiner feels that a telephone conference would be helpful, he is respectfully requested to call the undersigned attorney at the telephone number presented below.

It is believed that the rejections of record in the parent application, USSN 08/459,654, are not applicable to the pending claims. Accordingly, it is respectfully requested that favorable action on the new claims be taken.

Respectfully submitted,



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